REMARKS

A check for the feesfor a three month extension of time and a Notice of Appeal accompanies this response. Any fees that may be due in connection with the filing of this paper or with this application during its pendency may be charged to Deposit Account No. 06-1050. If a Petition for Extension of time is needed, this paper is to be considered such Petition.

The Examiner is thanked for her courtesy in granting an interview on April 20, 2006. The amendments and remarks provided herein are in accord with the Examiner's suggestions pursuant to the interview and address the issues raised in the Final Office Action.

Claims 8-14 and 58-73 are pending in this application. Claim 74 is cancelled without prejudice or disclaimer. The remaining claims (independent Claim 8 and Claim 58, rewritten herein as an independent claim) are amended herein, as discussed during the interview, to delete redundant language to thereby clarify that the transcription product is antisense to the target mRNA, *i.e.*, no additional antisense molecule other than the transcription product is recited in the claims. Claim 58 is rewritten as an independent claim incorporating the limitations of base Claim 8. All claims are rejected under 35 U.S.C. §112, second paragraph; only claims 8-14 are remain rejected over art under 35 U.S.C. §103(a).

It respectfully is submitted that entry of the amendments and consideration of the remarks should place the case into condition for allowance. For example, in the Final Office Action, Claim 58 and its dependents are rejected on grounds of indefiniteness but not on anticipation or obviousness grounds. Therefore, as discussed during the interview, addressing the indefiniteness issue as described above and rewriting the claim as an independent claim incorporating all the limitations of the base claim, should render Claim 58 and claims dependent thereon allowable.

Further, with respect to Claim 8 and its dependents, as discussed during the interview and herein and as made of record in the previous response filed August 3, 2005, neither of the references cited in the rejection on obviousness grounds (*i.e.*, Wagner *et al.* and Gudkov *et al.*), singly or in combination, teaches or suggests a high throughput method of assigning function to a target nucleic acid by circumventing tedious, discrete oligonucleotide design that is based on assessing accessibility of binding sites in a three dimensional conformational model of the target mRNA. Instead, as discussed during the interview and herein and as previously stated in the record, in the instant high throughput methods, the plurality of

oligonucleotide family members have sequences that are complementary to sequences that are distributed throughout the target mRNA, regardless of the three dimensional structure and binding site accessibility of the target mRNA. Therefore, it is respectfully submitted that the claims are patentable over the cited art and are allowable.

The amendment and response filed August 3, 2005, responsive to the previous Office Action (hereinafter, "previous response") is incorporated by reference in its entirety herein. No new matter is added.

STATEMENT OF THE SUBSTANCE OF THE INTERVIEW OF APRIL 20, 2006, WITH THE EXAMINER

Applicant thanks the Examiner for the courtesy extended in granting an interview to discuss specific issues raised in the Final Office Action of October 20, 2005. Pursuant to the discussion, Applicant further thanks the Examiner for agreeing to consider the instant Amendment after Final that incorporates the suggestions provided by the Examiner during the interview.

In the interview, Applicant and the Examiner discussed the two rejections set forth in the Final Office Action. In the first rejection, Claims 8-14 and 58-74 are rejected as being indefinite. Specifically, the Final Office Action alleges that the two recitations in the claims: (1) that the transcription products of the oligonucleotide family possess sequences that are complementary to the mRNA transcribed from the target nucleic acid; and (2) that the coding sequence for each transcription product encodes an antisense nucleic acid, makes it unclear whether the claim encompasses an "additional" antisense molecule because it appears that a sequence that is "complementary the mRNA" as recited in (1) already is "antisense" to the mRNA as recited in (2). Applicant proposed addressing this objection by removing the redundant language recited in (1), thereby clarifying that the claims do not recite an additional antisense molecule. The Examiner agreed that such an amendment would address the rejection on indefiniteness grounds.

In the second rejection, Claims 8-14 are rejected under 35 U.S.C. §103(a) as being unpatentable over Wagner *et al.* U.S. Patent No. 6,355,415, in view of Gudkov *et al.* U.S. Patent No. 5,753,432, for reasons of record, namely, that it would have been obvious to combine Wagner *et al.*, which allegedly teaches a method of assigning function to a sample nucleic acid by targeting ribozyme constructs that encompass antisense nucleic acid sequences to the sample nucleic acid and inhibiting production of a product encoded by the sample nucleic acid, with Gudkov *et al.*, which allegedly provides guidance for amplifying

and expressing oligonucleotide constructs without bacterial cloning steps, to arrive at the claimed subject matter.

During the interview, Applicant pointed out that the instant methods are "high throughput" by virtue of the design of oligonucleotide constructs that are complementary to sequences throughout the mRNA transcribed from the target nucleic acid of interest. One or more of these oligonucleotide constructs then bind to the target mRNA in a manner that inhibits its expression, resulting in a change in phenotype that is used to assign function to the target nucleic acid of interest. Applicant pointed out that the primary reference, Wagner *et al.*, on the other hand, teaches the design of discrete oligonucleotide constructs based on three dimensional conformational modeling of the target mRNA to look for accessible binding sites; the oligonucleotide molecules are designed to bind only to sites deemed accessible based on an assessment of the three dimensional computer modeled structure of the target mRNA. Applicant pointed out that Gudkov *et al.* also does not teach or suggest the design of an oligonucleotide family based on the primary sequence of a target mRNA, *i.e.*, without three dimensional computer modeling. Applicant explained that because neither reference teaches or suggests oligonucleotide family design based on the primary sequence and without three dimensional conformational modeling of mRNA transcribed from a target nucleic acid of interest, their combination cannot render the claims obvious. The Examiner then agreed to reconsider the rejection if Applicant clearly stated the aforementioned arguments in the amendment after Final.

At the conclusion of the interview, it was agreed that Applicant would provide an amended claim set and arguments, in accordance with the above suggestions, for the Examiner's review and consideration in an Amendment after Final. Applicant respectfully submits that, as discussed below, the instant Amendment after Final is compliant with the Examiner's suggestions as set forth during the interview. It is further submitted that the instant Amendment after Final is fully responsive to the Final Office Action of October 20, 2005, and either places the application in condition for allowance, or, alternatively, reduces the number of issues for appeal.

THE REJECTION OF CLAIMS 8-14 AND 58-74 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 8-14 and 58-74 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter. It is alleged that the metes and bounds of the claims are vague and indefinite because the nature of

the transcription product, which is recited as being complementary to the mRNA transcribed from the target nucleic acid of interest and is further recited as being an antisense nucleic acid that binds to the mRNA, is not clear. The Office Action further states that a transcription product that is complementary to the target mRNA already is "antisense" to the mRNA, therefore it is not clear whether the additional recitation of a transcription product that is antisense refers to an additional antisense molecule. Reconsideration and withdrawal of this rejection is respectfully requested. It respectfully is submitted that this rejection is rendered moot with respect to Claim 74, which is cancelled herein.

With regard to Claims 8-14 and 58-73, this rejection is obviated because the redundant language of these claims reciting that the transcription products are complementary to mRNA transcribed from the target nucleic acid, has been deleted. The claims as amended thus clarify that the "antisense" property refers to the individual transcription products of the oligonucleotide family and not to "additional" antisense molecules.

THE REJECTION OF CLAIMS 8-14 UNDER 35 U.S.C. §103(a)

Claims 8-14 remain rejected under 35 U.S.C. §103(a) as being unpatentable over Wagner *et al.* U.S. Patent No. 6,355,415 in view of Gudkov *et al.* U.S. Patent No. 5,753,432, for reasons of record. Responsive to Applicant's arguments responsive to the previous Office Action, in which Applicant asserted that the cited references and their combination do not teach or suggest the instant methods that are high throughput and does not rely on a discrete design and selection of oligonucleotide molecules, the Examiner alleges that to the contrary, the instant methods do rely on the sequence of the target mRNA and the oligonucleotide family is in fact designed based on the sequence of the target mRNA. Responsive to Applicant's argument that the instant methods do not rely on assessing a target mRNA structure for accessible binding sites, the Examiner alleges that this assertion reads away from the "very purpose of the claimed method," since the method requires an alteration in expression of the mRNA transcribed from the target nucleic acid in order to identify a function associated with it. This rejection is respectfully traversed. Reconsideration of this rejection is respectfully requested in view of the amendments herein and the following remarks.

ANALYSIS

The remarks and arguments made of record in the previous response filed August 3, 2005, are incorporated herein by reference. As discussed in the previous response, during the

interview and herein, in the primary reference, Wagner *et al.*, discrete ribozymes that will cleave a target mRNA of interest are identified by studying the secondary structure of the mRNA, by computer-based conformational modeling, for accessible cleavage sites. Wagner *et al.* does not teach or suggest any method of assigning function to a target nucleic acid without conformational modeling of the target mRNA. Further, the method of Wagner *et al.*, based on discrete selection by conformational modeling, is time-consuming and not amenable to a high-throughput screen. The secondary reference, Gudkov *et al.*, which teaches a random cDNA library used to identify heretofore unknown sequences that possess a certain function, also does not teach any oligonucleotide molecule design, discrete or otherwise, based on a known target mRNA. Therefore, Gudkov *et al.* does not cure the deficiencies of Wagner *et al.*

In the instant high throughput methods, the plurality of oligonucleotide family members have sequences that are complementary to sequences that are distributed throughout the target mRNA, regardless of the three dimensional structure and binding site accessibility of the target mRNA. The design of the oligonucleotide family is based on primary sequence of the target mRNA, rather than conformational modeling of its secondary structure.

The Examiner alleges that Applicant contradicted the "very purpose of the method" by allegedly arguing that in the instant methods, "it does not matter" if the members of the oligonucleotide family are effective antisense molecules. Applicant respectfully disagrees. Applicant argued that the instant methods, where the oligonucleotide family members are designed based on primary sequence of the mRNA target, offer a high throughput, "shotgun" type approach where, as the claims recite, one or members of the family bind to the target mRNA in a manner that inhibits its expression, resulting in a change in phenotype that is used to assign function to the target nucleic acid of interest.

Neither of the cited references teaches or suggests a method in which an oligonucleotide family is designed based on the primary sequence and without three dimensional conformational modeling of mRNA transcribed from a target nucleic acid of interest. Therefore, their combination cannot render the claims obvious. Therefore, the Examiner has failed to set forth a *prima facie* case of obviousness.

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In view of the above, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,

Stephanie L. Seidman
Reg. No. 33,779

Attorney Docket No. 17111-007US1/2307US
Address all correspondence to:
Stephanie Seidman
Fish & Richardson P.C.
12390 El Camino Real
San Diego, California 92130
Telephone: (858) 678-5070
Facsimile: (202) 626-7796
email:seidman@fr.com